

WHAT IS CLAIMED IS:

1. A genetically modified rodent animal comprising in its genome:

a humanized Tslp gene comprising:

a rodent Tslp nucleic acid sequence, and

a human TSLP nucleic acid sequence,

wherein the humanized Tslp gene encodes a humanized Tslp polypeptide comprising a mature protein sequence having at least 95% identity substantially identical to the mature protein sequence of a human TSLP protein; and

wherein the rodent animal is a mouse or a rat.
- ~~2. The genetically modified rodent animal of claim 1, wherein the humanized Tslp polypeptide comprises a mature protein sequence having at least 95% identity to the mature protein sequence of the human TSLP protein.~~
- ~~3. The genetically modified rodent animal of claim 1, wherein the humanized Tslp polypeptide comprises a mature protein sequence identical to the mature protein sequence of the human TSLP protein.~~
- ~~4. The genetically modified rodent animal of any one of claims 1-3, wherein the humanized Tslp protein comprises a signal peptide substantially identical to the signal peptide of a rodent Tslp protein.~~
- ~~5. The genetically modified rodent animal of claim 4, wherein the humanized Tslp protein comprises a signal peptide having at least 95% identity to the signal peptide of a rodent Tslp protein.~~
62. The genetically modified rodent animal of claim 41, wherein the humanized Tslp ~~polypeptide~~protein comprises a signal peptide identical to the signal peptide of a rodent Tslp protein such as an endogenous rodent Tslp protein.

~~7. — The genetically modified rodent animal of any one of the preceding claims, wherein the human TSLP nucleic acid sequence encodes at least a substantial portion of the mature protein sequence of the human TSLP protein.~~

~~8. — The genetically modified rodent animal of claim 7, wherein the human TSLP nucleic acid sequence encodes the mature protein sequence of the human TSLP protein.~~

93. The genetically modified rodent animal of claim ~~8~~1 or 2, wherein the human TSLP nucleic acid sequence comprises exon 1 from the codon for the first amino acid of the mature protein sequence, through the STOP codon in exon 4, of a human TSLP gene.

~~10. — The genetically modified rodent animal of any one of claims 1-9, wherein the rodent Tslp nucleic acid sequence comprises exonic sequences of a rodent Tslp gene that encode the rodent Tslp signal peptide.~~

~~114.~~ The genetically modified rodent animal of any one of claims 1-3~~claim 10~~, wherein the rodent animal is a mouse, and the rodent nucleic acid sequence comprises exon 1, and a 5' portion of exon 2 coding for signal peptide amino acids, of a mouse Tslp gene.

~~125.~~ The genetically modified rodent animal of any one of claims 1-~~49~~, wherein the rodent Tslp nucleic acid sequence comprises the 3' UTR of a rodent Tslp gene such as an endogenous rodent Tslp gene.

~~13. — The genetically modified rodent animal of any one of claims 10-12, wherein the rodent Tslp gene is an endogenous Tslp gene.~~

~~146.~~ The genetically modified rodent animal of claim 1, wherein the rodent animal is a mouse, and the humanized Tslp gene comprises (i) exon 1, and a 5' portion of exon 2 coding for signal peptide amino acids, of a mouse Tslp gene, and (ii) exon 1 from the codon for the first amino acid of the mature protein sequence, through the STOP codon in exon 4, of a human TSLP gene, and optionally (iii) the 3' UTR of the mouse Tslp gene.

~~15. — The genetically modified rodent animal of claim 14, wherein the humanized Tslp gene further comprises the 3' UTR of the mouse Tslp gene.~~

~~167.~~ The genetically modified rodent animal of any one of claims 1-~~156~~, wherein the humanized Tslp gene is operably linked to a rodent Tslp promoter such as an endogenous rodent Tslp promoter.

~~17.~~—~~The genetically modified rodent animal of claim 16, wherein the rodent Tslp promoter is the endogenous rodent Tslp promoter.~~

~~188.~~ The genetically modified rodent animal of any one of claims 1-~~177~~, wherein the humanized Tslp gene is located at an endogenous rodent Tslp locus.

~~19.~~—~~The genetically modified rodent animal of claim 18, wherein the humanized Tslp gene is formed as a result of replacement of a rodent Tslp genomic DNA at an endogenous rodent Tslp locus with the human TSLP nucleic acid.~~

~~20.~~—~~The genetically modified rodent animal of claim 19, wherein the humanized Tslp gene is formed as a result of replacement of a rodent genomic DNA comprising exonic sequences encoding at least a substantial portion of the mature protein sequence of the endogenous rodent Tslp protein, with the human TSLP nucleic acid which encodes at least a substantial portion of the mature protein sequence of the human TSLP protein.~~

~~21.~~—~~The genetically modified rodent animal of claim 20, wherein the humanized Tslp gene is formed as a result of replacement of a rodent genomic DNA comprising exonic sequences encoding the mature protein sequence of the endogenous rodent Tslp protein, with the human TSLP nucleic acid which encodes the mature protein sequence of the human TSLP protein.~~

~~229.~~ The genetically modified rodent animal of claim ~~218~~, wherein the rodent animal is a mouse, and wherein the mouse genomic DNA being replaced comprises exon 2 from the codon for the first amino acid of the mature mouse Tslp protein through the STOP codon in exon 5 of the endogenous mouse Tslp gene, and the human genomic DNA comprises exon 1 from the codon for the first amino acid of the mature human TSLP protein through the STOP codon in exon 4 of a human TSLP gene.

~~2310.~~ The genetically modified rodent animal of any of claims 1-~~229~~, wherein the rodent is homozygous for the humanized Tslp gene.

~~2411.~~ The genetically modified rodent animal of any of claims 1-~~229~~, wherein the rodent is heterozygous for the humanized Tslp gene.

~~25. The genetically modified rodent animal of any of the preceding claims, wherein the rodent expresses the humanized Tslp polypeptide.~~

~~2612.~~ The genetically modified rodent animal of any of the preceding claims, whose genome further comprises a humanized Tslpr gene at an endogenous rodent Tslpr locus, a humanized Il7ra gene at an endogenous rodent Il7ra locus, or a combination thereof.

~~27. The genetically modified rodent animal of any of the preceding claims, wherein the rodent is a mouse or a rat.~~

~~2813.~~ An isolated rodent tissue or cell, whose genome comprises a humanized Tslp gene comprising a rodent Tslp nucleic acid sequence and a human TSLP nucleic acid sequence, wherein the humanized Tslp gene encodes a humanized Tslp polypeptide comprising a mature protein sequence having at least 95% identity substantially identical to a mature protein sequence of a human TSLP protein, and wherein the rodent is mouse or rat.

~~29. The isolated rodent tissue or cell of claim 28, wherein the humanized Tslp polypeptide comprises a mature protein sequence having at least 95% identity to a mature protein sequence of a human TSLP protein.~~

~~3014.~~ The isolated rodent tissue or cell of claim ~~28 or 2914~~, wherein the rodent cell is a rodent embryonic stem cell.

~~31. The isolated rodent tissue or cell of any one of claims 28-30, wherein the rodent is a mouse or a rat.~~

~~3215.~~ A rodent embryo, comprising the rodent embryonic stem cell of claim ~~3014~~.

~~3316.~~ A method of making a genetically modified rodent, comprising:

modifying a rodent genome to comprise a humanized Tslp gene, wherein the humanized Tslp gene comprises a rodent Tslp nucleic acid sequence and a human TSLP nucleic acid

sequence, and encodes a humanized Tslp polypeptide comprising a mature protein sequence having at least 95% identity substantially identical with the mature protein sequence of a human TSLP protein; and

making a rodent comprising the modified rodent genome;

wherein the rodent is mouse or rat.

~~34. The method of claim 33, wherein the humanized Tslp polypeptide comprises a mature protein sequence having at least 95% identity with the mature protein sequence of a human TSLP protein.~~

~~35~~17. The method of claim ~~33 or 34~~16, wherein said modifying comprises

introducing a nucleic acid molecule comprising the human TSLP nucleic acid sequence into the genome of a rodent embryonic stem (ES) cell,

obtaining a rodent ES cell in which the human TSLP nucleic acid sequence has been integrated into an endogenous Tslp locus to replace a rodent Tslp genomic DNA thereby forming the humanized Tslp gene, and

generating a rodent animal from the obtained rodent ES cell.

~~36. The method of claim 35, wherein the nucleic acid molecule further comprises a 5' homology arm and a 3' homology arm flanking the human TSLP nucleic acid sequence, and wherein the 5' and 3' homology arms are homologous to nucleic acid sequences at the endogenous rodent locus flanking the rodent Tslp genomic DNA to be replaced.~~

~~37~~18. The method of claim ~~35 or 36~~17, wherein the humanized Tslp gene is operably linked to the endogenous rodent Tslp promoter at the endogenous rodent Tslp locus.

~~38. The method of any one of claims 33-37, wherein the human TSLP nucleic acid sequence encodes at least a substantial portion of the mature protein sequence of the human TSLP protein.~~

~~39. The method of any one of claims 33-38, wherein the rodent is a mouse or a rat.~~

~~40~~19. A targeting nucleic acid construct, comprising

a human TSLP nucleic acid sequence to be integrated into a rodent Tslp gene at an endogenous rodent Tslp locus, flanked by a 5' nucleotide sequence and a 3' nucleotide sequence that are homologous to nucleotide sequences at the rodent Tslp locus,

wherein integration of the human TSLP nucleic acid sequence into the rodent Tslp gene results in a replacement of a rodent Tslp genomic DNA with the human TSLP nucleic acid sequence thereby forming a humanized Tslp gene, ~~and~~

wherein the human TSLP nucleic acid sequence encodes ~~at least a substantial portion of~~ the mature protein sequence of a human TSLP protein, ~~and~~

~~wherein the rodent is mouse or rat.~~

~~41. —The targeting nucleic acid of claim 40, wherein the rodent is a mouse or a rat.~~

~~42~~20. A genetically modified rodent animal comprising in its genome:

a humanized Tslpr gene comprising:

a rodent Tslpr nucleic acid sequence, and

a human TSLPR nucleic acid sequence,

wherein the humanized Tslpr gene encodes a humanized Tslpr polypeptide comprising an ectodomain ~~having at least 95% identity substantially identical~~ to the ectodomain of a human TSLPR protein, ~~and~~

~~wherein the rodent animal is a mouse or a rat.~~

~~43. —The genetically modified rodent animal of claim 42, wherein the humanized Tslpr protein comprises an ectodomain having at least 95% identity to the ectodomain of a human TSLPR protein.~~

~~44. —The genetically modified rodent animal of claim 42, wherein the humanized Tslpr protein comprises an ectodomain identical to the ectodomain of a human TSLPR protein.~~

~~4521.~~ The genetically modified rodent animal of ~~any one of claims 42-44~~claim 20, wherein the humanized Tslpr ~~protein~~polypeptide comprises a transmembrane-cytoplasmic sequence having at least 95% identity substantially identical to the transmembrane-cytoplasmic sequence of a rodent Tslpr protein such as an endogenous rodent Tslpr protein.

~~46.—The genetically modified rodent animal of claim 45, wherein the humanized Tslpr protein comprises a transmembrane-cytoplasmic sequence having at least 95% identity to the transmembrane-cytoplasmic sequence of a rodent Tslpr protein.~~

~~47.—The genetically modified rodent animal of claim 46, wherein the humanized Tslpr protein comprises the transmembrane-cytoplasmic sequence of an endogenous rodent Tslpr protein.~~

~~48.—The genetically modified rodent animal of any one of claims 42-47, wherein the humanized Tslpr protein comprises a signal peptide substantially identical to the signal peptide of a rodent Tslpr protein.~~

~~49.—The genetically modified rodent animal of claim 48, wherein the humanized Tslpr protein comprises a signal peptide having at least 95% identity to the signal peptide of a rodent Tslpr protein.~~

~~5022.~~ The genetically modified rodent animal of claim ~~49~~20 or 21, wherein the humanized Tslpr ~~polypeptide~~protein comprises the signal peptide of a rodent Tslpr protein such as an endogenous rodent Tslpr protein.

~~51.—The genetically modified rodent animal of any one of claims 40-50, wherein the human TSLPR nucleic acid sequence encodes at least a substantial portion of the ectodomain of the human TSLPR protein.~~

~~5223.~~ The genetically modified rodent animal of ~~claim 51~~any one of claims 20-22, wherein the human TSLPR nucleic acid sequence comprises exon 2 through the codon for the last ectodomain amino acid in exon 6 of a human TSLPR gene.

~~53. The genetically modified rodent animal of any one of claims 40-52, wherein the rodent Tslpr nucleic acid sequence comprises exonic sequences of a rodent Tslpr gene that encode at least a substantial portion of the transmembrane-cytoplasmic sequence of a rodent Tslpr protein.~~

~~54~~24. The genetically modified rodent animal of ~~claim 53~~any one of claims 20-23, wherein the rodent animal is a mouse, and the rodent Tslpr nucleic acid sequence comprises exon 6 from the codon for the first amino acid of the transmembrane domain through exon 8 of a mouse Tslpr gene.

~~55. The genetically modified rodent animal of any one of claims 40-54, wherein the rodent Tslpr nucleic acid sequence comprises exonic sequences of a rodent Tslpr gene that encode the signal peptide of a rodent Tslpr protein.~~

~~56~~25. The genetically modified rodent animal of ~~claim 55~~any one of claims 20-24, wherein the rodent animal is a mouse, and the rodent nucleic acid sequence comprises exon 1 of a mouse Tslpr gene.

~~57. The genetically modified rodent animal of any one of claims 53-56, wherein the rodent Tslpr gene is an endogenous Tslpr gene.~~

~~58~~26. The genetically modified rodent animal of claim ~~40~~20, wherein the rodent animal is a mouse, and the humanized Tslpr gene comprises (i) exon 1 of a mouse Tslpr gene, (ii) exon 2 through the codon for the last amino acid of the ectodomain in exon 6 of a human TSLPR gene; and (iii) exon 6 from the codon for the first amino acid of the transmembrane domain through exon 8 of the mouse Tslpr gene.

~~59~~27. The genetically modified rodent animal of any one of claims ~~40-58~~20-26, wherein the humanized Tslpr gene is operably linked to a rodent Tslpr promoter such as an endogenous rodent Tslpr promoter.

~~60. The genetically modified rodent animal of claim 59, wherein the rodent Tslpr promoter is the endogenous rodent Tslpr promoter.~~

~~61~~28. The genetically modified rodent animal of any one of claims ~~40-60~~20-27, wherein the humanized Tslpr gene is located at an endogenous rodent Tslpr locus.

~~6229.~~ The genetically modified rodent animal of claim ~~6128~~, wherein the humanized Tslpr gene is ~~formed as~~ a result of replacement of a rodent Tslpr genomic DNA at an endogenous rodent Tslpr locus with the human TSLPR nucleic acid.

~~63.—The genetically modified rodent animal of claim 62, wherein the humanized Tslpr gene is formed as a result of replacement of a rodent genomic DNA comprising exonic sequences encoding at least a substantial portion of the ectodomain of the endogenous rodent Tslpr protein, with the human TSLPR nucleic acid which encodes at least a substantial portion of the ectodomain of the human TSLPR protein.~~

~~6430.~~ The genetically modified rodent animal of claim ~~6329~~, wherein the rodent animal is a mouse, and wherein the mouse genomic DNA being replaced comprises exon 2 through the codon for the last amino acid of the ectodomain in exon 6 of the endogenous mouse Tslpr gene, and the human genomic DNA comprises exon 2 through the codon for the last amino acid of the ectodomain in exon 6 of a human TSLPR gene.

~~6531.~~ The genetically modified rodent animal of any of claims ~~40-6420-30~~, wherein the rodent is homozygous for the humanized Tslpr gene.

~~6632.~~ The genetically modified rodent animal of any of claims ~~40-6220-30~~, wherein the rodent is heterozygous for the humanized Tslpr gene.

~~67.—The genetically modified rodent animal of any of claims 40-66, wherein the rodent expresses the humanized Tslpr polypeptide.~~

~~6833.~~ The genetically modified rodent animal of any of claims ~~40-6720-32~~, whose genome further comprises a humanized Tslp gene at an endogenous rodent Tslp locus, a humanized Il7ra gene at an endogenous rodent Il7ra locus, or a combination thereof.

~~69.—The genetically modified rodent animal of any of claims 40-68, wherein the rodent is a mouse or a rat.~~

~~7034.~~ An isolated rodent tissue or cell, whose genome comprises a humanized Tslpr gene comprising a rodent Tslpr nucleic acid sequence and a human TSLPR nucleic acid sequence,

wherein the humanized Tslpr gene encodes a humanized Tslpr polypeptide comprising an ectodomain having at least 95% identity substantially identical to the ectodomain of a human TSLPR protein, and wherein the rodent is mouse or rat.

~~71. The isolated rodent tissue or cell of claim 70, wherein the humanized Tslpr polypeptide comprises an ectodomain having at least 95% identity to the ectodomain of a human TSLPR protein.~~

~~7235.~~ The isolated rodent tissue or cell of claim ~~70 or 7134~~, wherein the rodent cell is a rodent embryonic stem cell.

~~73. The isolated rodent tissue or cell of any of claims 70-72, wherein the rodent is a mouse or a rat.~~

~~7436.~~ A rodent embryo, comprising the rodent embryonic stem cell of claim ~~7235~~.

~~7537.~~ A method of making a genetically modified rodent, comprising:

modifying a rodent genome to comprise a humanized Tslpr gene, wherein the humanized Tslpr gene comprises a rodent Tslpr nucleic acid sequence and a human TSLPR nucleic acid sequence, and encodes a humanized Tslpr polypeptide comprising an ectodomain having at least 95% identity substantially identical with the ectodomain of a human TSLP protein; and

making a rodent comprising the modified rodent genome;

wherein the rodent is mouse or rat.

~~76. The method claim 75, wherein the humanized Tslpr polypeptide comprises an ectodomain having at least 95% identity with the ectodomain of a human TSLP protein.~~

~~7738.~~ The method of claim ~~75 or 7637~~, wherein said modifying comprises

introducing a nucleic acid molecule comprising the human TSLPR nucleic acid sequence into the genome of a rodent embryonic stem (ES) cell,

obtaining a rodent ES cell in which the human TSLPR nucleic acid sequence has been integrated into an endogenous Tslpr locus to replace a rodent Tslpr genomic DNA thereby forming the humanized Tslpr gene, and

generating a rodent animal from the obtained rodent ES cell.

~~78. — The method of claim 75, wherein the nucleic acid molecule further comprises a 5' homology arm and a 3' homology arm flanking the human TSLPR nucleic acid sequence, and wherein the 5' and 3' homology arms are homologous to nucleic acid sequences at the endogenous rodent locus flanking the rodent Tslpr genomic DNA to be replaced. —~~

~~79~~39. The method of claim ~~77 or 78~~37 or 38, wherein the humanized Tslpr gene is operably linked to the endogenous rodent Tslpr promoter at the endogenous rodent Tslpr locus.

~~80. — The method of any one of claims 75-79, wherein the human TSLPR nucleic acid sequence encodes at least a substantial portion of the ectodomain of the human TSLPR protein.~~

~~81. — The method of any one of claims 75-80, wherein the rodent is a mouse or a rat.~~

~~82~~40. A targeting nucleic acid construct, comprising

a human TSLPR nucleic acid sequence to be integrated into a rodent Tslpr gene at an endogenous rodent Tslpr locus, flanked by a 5' nucleotide sequence and a 3' nucleotide sequence that are homologous to nucleotide sequences at the rodent Tslpr locus,

wherein integration of the human TSLPR nucleic acid sequence into the rodent Tslpr gene results in a replacement of a rodent Tslpr genomic DNA with the human TSLPR nucleic acid sequence thereby forming a humanized Tslpr gene, ~~and~~

wherein the human TSLPR nucleic acid sequence encodes at least a substantial portion of the ectodomain of a human TSLPR protein,

wherein the humanized Tslpr gene encodes a humanized Tslpr polypeptide comprising an ectodomain having at least 95% identity with the ectodomain of a human TSLP protein, and

wherein the rodent is mouse or rat.

~~83. —The targeting nucleic acid of claim 82, wherein the rodent is a mouse or a rat.~~

~~8441.~~ A genetically modified rodent animal comprising in its genome:

a humanized IL7ra gene comprising:

a rodent IL7ra nucleic acid sequence, and

a human IL7RA nucleic acid sequence,

wherein the humanized IL7ra gene encodes a humanized IL7ra polypeptide comprising an ectodomain having at least 95% identity substantially identical to the ectodomain of a human IL7RA protein, and

wherein the rodent animal is a mouse or a rat.

~~85. —The genetically modified rodent animal of claim 84, wherein the humanized IL7ra polypeptide comprises an ectodomain having at least 95% identity to the ectodomain of a human IL7RA protein.~~

~~86. —The genetically modified rodent animal of claim 84, wherein the humanized IL7ra polypeptide comprises an ectodomain identical to the ectodomain of a human IL7RA protein.~~

~~8742.~~ The genetically modified rodent animal of ~~any one of claims 84-86~~claim 41, wherein the humanized IL7ra ~~polypeptide~~protein comprises a transmembrane-cytoplasmic sequence having at least 95% identity~~substantially identical~~ to the transmembrane-cytoplasmic sequence of a rodent IL7ra protein such as an endogenous rodent IL7ra protein.

~~88. —The genetically modified rodent animal of claim 87, wherein the humanized IL7ra protein comprises a transmembrane-cytoplasmic sequence having at least 95% identity to the transmembrane-cytoplasmic sequence of a rodent IL7ra protein.~~

~~89. The genetically modified rodent animal of claim 87, wherein the humanized IL7ra protein comprises the transmembrane-cytoplasmic sequence of an endogenous rodent IL7ra protein.~~

~~90~~43. The genetically modified rodent animal of ~~any one of claims 84-89~~claim 41 or 42, wherein the humanized IL7ra ~~polypeptide~~protein comprises ~~a signal peptide substantially identical to~~ the signal peptide of a rodent IL7ra protein such as an endogenous rodent IL7ra protein.

~~91. The genetically modified rodent animal of claim 90, wherein the humanized IL7ra protein comprises a signal peptide having at least 95% identity to the signal peptide of a rodent IL7ra protein.~~

~~92. The genetically modified rodent animal of claim 90, wherein the humanized IL7ra protein comprises the signal peptide of an endogenous rodent IL7ra protein.~~

~~93. The genetically modified rodent animal of any one of claims 84-92, wherein the human IL7RA nucleic acid sequence encodes at least a substantial portion of the ectodomain of the human IL7RA protein.~~

~~94~~44. The genetically modified rodent animal of ~~claim 93~~any one of claims 41-43, wherein the human IL7RA nucleic acid sequence comprises from the codon in exon 2 encoding the first amino acid of the mature human IL7RA protein through exon 5 of a human IL7RA gene.

~~95. The genetically modified rodent animal of any one of claims 84-94, wherein the rodent IL7ra nucleic acid sequence comprises exonic sequences of a rodent IL7ra gene that encode at least a substantial portion of the transmembrane-cytoplasmic sequence of a rodent IL7ra protein.~~

~~96~~45. The genetically modified rodent animal ~~of claim 95~~any one of claims 41-44, wherein the rodent animal is a mouse, and the rodent IL7ra nucleic acid sequence comprises exon 6 through exon 8 of a mouse IL7ra gene.

~~97~~46. The genetically modified rodent animal of any one of claims ~~84-96~~41-45, wherein the rodent IL7ra nucleic acid sequence comprises the portion in exon 1 of a rodent IL7ra gene that encodes the signal peptide of a rodent IL7ra protein such as an endogenous rodent IL7ra protein.

~~9847.~~ The genetically modified rodent animal of claim ~~9746~~, wherein the rodent Il7ra nucleic acid sequence comprises the 5' UTR portion of exon 1 of the rodent Il7ra gene such as an endogenous rodent Il7ra gene.

~~99.—The genetically modified rodent animal of any one of claims 95-98, wherein the rodent Il7ra gene is an endogenous Il7ra gene.~~

~~10048.~~ The genetically modified rodent animal of claim ~~8441~~, wherein the rodent animal is a mouse, and the humanized Il7ra gene comprises (i) a portion of exon 1 of a mouse Il7ra gene comprising the 5' UTR and the sequence encoding the signal peptide of the mouse Il7ra, (ii) the codon in exon 1 of a human IL7RA gene that encodes the first amino acid of the mature human IL7RA protein through exon 5 of the human IL7RA gene; and (iii) exon 6 in through exon 8 of the mouse Il7ra gene.

~~10149.~~ The genetically modified rodent animal of any one of claims ~~84-10041-48~~, wherein the humanized Il7ra gene is operably linked to a rodent Il7ra promoter such as an endogenous rodent Il7ra promoter.

~~101.—The genetically modified rodent animal of claim 101, wherein the rodent Il7ra promoter is the endogenous rodent Il7ra promoter.~~

~~10250.~~ The genetically modified rodent animal of any one of claims ~~84-10141-49~~, wherein the humanized Il7ra gene is located at an endogenous rodent Il7ra locus.

~~10351.~~ The genetically modified rodent animal of claim ~~10250~~, wherein the humanized Il7ra gene is ~~formed as~~ a result of replacement of a rodent Il7ra genomic DNA at an endogenous rodent Il7ra locus with the human IL7RA nucleic acid.

~~104.—The genetically modified rodent animal of claim 103, wherein the humanized Il7ra gene is formed as a result of replacement of a rodent genomic DNA comprising exonic sequences encoding at least a substantial portion of the ectodomain of the endogenous rodent Il7ra protein, with the human IL7RA nucleic acid which encodes at least a substantial portion of the ectodomain of the human IL7RA protein.~~

~~105~~52. The genetically modified rodent animal of claim ~~105~~51, wherein the rodent animal is a mouse, and wherein the mouse genomic DNA being replaced comprises the codon in exon 1 encoding the first amino acid of the mature mouse Il7ra protein through exon 5 of the endogenous mouse Il7ra gene, and the human genomic DNA comprises the codon in exon 1 encoding the first amino acid of the mature human IL7RA protein through exon 5 of a human IL7RA gene.

~~106~~53. The genetically modified rodent animal of any of claims ~~84-105~~41-52, wherein the rodent is homozygous for the humanized Il7ra gene.

~~107~~54. The genetically modified rodent animal of any of claims ~~84-105~~41-52, wherein the rodent is heterozygous for the humanized Il7ra gene.

~~108. The genetically modified rodent animal of any of claims 84-107, wherein the rodent expresses the humanized Il7ra polypeptide.~~

~~109~~55. The genetically modified rodent animal of any of claims ~~84-108~~41-54, whose genome further comprises a humanized Tslp gene at an endogenous rodent Tslp locus, a humanized Tslpr gene at an endogenous rodent Tslpr locus, or a combination thereof.

~~110. The genetically modified rodent animal of any of claims 84-109, wherein the rodent is a mouse or a rat.~~

~~111~~56. An isolated rodent tissue or cell, whose genome comprises a humanized Il7ra gene comprising a rodent Il7ra nucleic acid sequence and a human IL7RA nucleic acid sequence, wherein the humanized Il7ra gene encodes a humanized Il7ra polypeptide comprising an ectodomain having at least 95% identity substantially identical to the ectodomain of a human IL7RA protein, wherein the rodent is mouse or rat.

~~112. The isolated rodent tissue or cell of claim 111, wherein the humanized Il7ra polypeptide comprises an ectodomain having at least 95% identity to the ectodomain of a human IL7RA protein.~~

~~11357.~~ The isolated rodent tissue or cell of claim ~~111 or 112~~56, wherein the rodent cell is a rodent embryonic stem cell.

~~114. The isolated rodent tissue or cell of any one of claims 111-113, wherein the rodent is a mouse or a rat.~~

~~115~~58. A rodent embryo, comprising the rodent embryonic stem cell of claim ~~113~~56.

~~116~~59. A method of making a genetically modified rodent, comprising:

modifying a rodent genome to comprise a humanized Il7ra gene, wherein the humanized Il7ra gene comprises a rodent Il7ra nucleic acid sequence and a human IL7RA nucleic acid sequence, and encodes a humanized Il7ra polypeptide comprising an ectodomain having at least 95% identity~~substantially identical~~ with the ectodomain of a human IL7RA protein; and

making a rodent comprising the modified rodent genome;

wherein the rodent is mouse or rat.

~~117. The method of claim 116, wherein the humanized Il7ra polypeptide comprises an ectodomain having at least 95% identity to the ectodomain of a human IL7RA protein.~~

~~118~~60. The method of claim ~~116 or 117~~59, wherein said modifying comprises

introducing a nucleic acid molecule comprising the human IL7RA nucleic acid sequence into the genome of a rodent embryonic stem (ES) cell,

obtaining a rodent ES cell in which the human IL7RA nucleic acid sequence has been integrated into an endogenous Il7ra locus to replace a rodent Il7ra genomic DNA thereby forming the humanized Il7ra gene, and

generating a rodent animal from the obtained rodent ES cell.

~~119. The method of claim 118, wherein the nucleic acid molecule further comprises a 5' homology arm and a 3' homology arm flanking the human IL7RA nucleic acid sequence, and~~

~~wherein the 5' and 3' homology arms are homologous to nucleic acid sequences at the endogenous rodent locus flanking the rodent Il7ra genomic DNA to be replaced.~~

~~120~~61. The method of claim ~~118 or 119~~60, wherein the humanized Il7ra gene is operably linked to the endogenous rodent Il7ra promoter at the endogenous rodent Tslpr locus.

~~121. The method of any one of claims 116-120, wherein the human IL7RA nucleic acid sequence encodes at least a substantial portion of the ectodomain of the human IL7RA protein.~~

~~122. The method of any one of claims 116-121, wherein the rodent is a mouse or a rat.~~

~~123~~62. A targeting nucleic acid construct, comprising

a human IL7RA nucleic acid sequence to be integrated into a rodent Il7ra gene at an endogenous rodent Il7ra locus, flanked by a 5' nucleotide sequence and a 3' nucleotide sequence that are homologous to nucleotide sequences at the rodent Il7ra locus,

wherein integration of the human IL7RA nucleic acid sequence into the rodent Il7ra gene results in a replacement of a rodent Il7ra genomic DNA with the human IL7RA nucleic acid sequence thereby forming a humanized Il7ra gene, ~~and~~

wherein the human IL7RA nucleic acid sequence encodes at least a substantial portion of the ectodomain of a human IL7RA protein,

wherein the humanized Il7ra gene encodes a humanized Il7ra polypeptide comprising an ectodomain having at least 95% identity to the ectodomain of a human IL7RA protein, and

wherein the rodent is mouse or rat.

~~124. The targeting nucleic acid of claim 123, wherein the rodent is a mouse or a rat.~~

~~125~~63. A genetically modified rodent of any one of claims 1-~~122~~7, ~~42-69~~20-33, or ~~84-110~~41-55, further comprising a humanized Sirp α gene, wherein the rodent is homozygous for RAG2^{-/-} and IL2RG^{-/-}.

~~12664~~. A genetically modified rodent of claim ~~12563~~, wherein the rodent further comprises a humanized Tpo gene, and/or a humanized GM-CSF/IL-3 locus.

~~12765~~. Use of a genetically modified rodent animal as defined by any of claims 1-~~2712~~, ~~42-6920-33~~, ~~84-11041-55~~, or ~~125-12663-64~~ in the preparation of a rodent animal model of allergic diseases (e.g., asthma or skin inflammation) or cancer.

~~128. — A method of testing a candidate agent for treating an allergic condition, comprising inducing an allergic condition in a genetically modified rodent animal as defined by any of claims 1-27, 42-69, 84-110 or 125-126; administering a candidate agent to the genetically modified rodent animal; and determining whether the candidate agent inhibits the allergic condition in the genetically modified rodent animal. —~~

~~129. — A method of testing a candidate agent for treating cancer, comprising engrafting human cancer cells in a genetically modified rodent animal as defined by any of claims 1-27, 42-69, 84-110, or 125-126; administering a candidate agent to the genetically modified rodent animal; and determining whether the candidate agent inhibits the growth of the cancer cells in the genetically modified rodent animal. —~~

~~130. — The method of claim 128 or 129, wherein the candidate agent is a small molecule compound, a nucleic acid, or an antibody.~~

~~13166~~. An *in vitro* method for generating a genetically modified rodent cell, comprising introducing the targeting nucleic acid construct of claim ~~40 or 4119~~ into a rodent cell, whereby the human TSLP nucleic acid sequence is integrated into the endogenous rodent Tslp gene resulting in a replacement of a rodent Tslp genomic DNA with the human TSLP nucleic acid sequence to form a humanized Tslp gene, thereby generating the genetically modified rodent cell, wherein optionally the rodent cell is a rodent ES cell.

~~132. — The method of claim 131, wherein the rodent cell is a rodent ES cell.~~

~~13367~~. An *in vitro* method for generating a genetically modified rodent cell, comprising

introducing the targeting nucleic acid construct of claim ~~82 or 83~~40 into a rodent cell, whereby the human TSLPR nucleic acid sequence is integrated into the endogenous rodent Tslpr gene resulting in a replacement of a rodent Tslpr genomic DNA with the human TSLPR nucleic acid sequence to form a humanized Tslpr gene, thereby generating the genetically modified rodent cell, wherein optionally the rodent cell is a rodent ES cell.

~~134. The method of claim 133, wherein the rodent cell is a rodent ES cell.~~

~~135~~68. An *in vitro* method for generating a genetically modified rodent cell, comprising

introducing the targeting nucleic acid construct of claim ~~123 or 124~~62 into a rodent cell, whereby the human IL7RA nucleic acid sequence is integrated into the endogenous rodent Il7ra gene resulting in a replacement of a rodent Il7ra genomic DNA with the human IL7RA nucleic acid sequence to form a humanized Il7ra gene, thereby generating the genetically modified rodent cell, wherein optionally the rodent cell is a rodent ES cell.

~~136. The method of claim 135, wherein the rodent cell is a rodent ES cell.~~